

Remarks

Claims 10-13, 47 and 48 were pending in the subject application. By this Amendment, the applicants have amended claims 10, 11, and 13, cancelled claims 1-6, 8, 9, 14-19, 21-38, 40-42 and 44-48 as being drawn to non-elected subject matter, and added new claims 49 and 50. Support for the amendments to the claims can be found throughout the specification and claims as filed and at, for example, page 28, last paragraph to 29, 2nd paragraph, page 19, last paragraph, and Figures 1-2 and 4-6. No new matter has been added by these amendments. Accordingly, claims 10-11, 13, 49 and 50 are before the Examiner for consideration.

The amendments to the claims have been made to lend greater clarity to the claimed subject matter and to expedite prosecution. The amendments should not be taken to indicate the applicants' agreement with, or acquiescence to, the rejections of record. Favorable consideration of the claims now presented, in view of the remarks and amendments set forth herein, is earnestly solicited.

Claims 10-13, 47 and 48 have been rejected under 35 U.S.C. §112, first paragraph, as not being enabling for the full scope of the claims. The applicants respectfully traverse this ground for rejection to the extent that it might be applied to the claims now presented for examination. The diagnostic methods, as currently-claimed, could be readily practiced by the skilled artisan without any need for undue experimentation.

To satisfy enablement under §112 the specification need only teach a person of ordinary skill in the art how to make and how to use the full scope of the invention without undue experimentation. The requirement for some experimentation and/or screening does not necessarily make a claim non-enabled. "Enablement is not precluded by the necessity for some experimentation such as routine screening A considerable amount of experimentation is permissible, if it is merely routine" (emphasis added). *In re Wands*, 8 USPQ 2d 1400, 1404 (Fed. Cir. 1988).

One skilled in the art could readily, and without undue experimentation, utilize the methods of the subject invention for 1) predicting whether a tumor is likely to metastasize; and 2) diagnosing whether a subject has cancer. These diagnostic methods can be applied to various

types of cancer including, for example, the cancer of intestines (including the colon and rectum), as well as breast cancer, lung cancer, brain cancer, bone cancer, and gastric cancer.

The specification teaches that 7a5/Prognostin is expressed at higher levels in cancer patients, and is especially high in those subjects who are undergoing, or will develop, metastatic spread of the cancer (specification at page 3 and page 19, last paragraph). Experimental results are presented in the specification that demonstrate that the transcriptional expression of 7a5/Prognostin is a) higher in malignant tissues than in corresponding healthy tissues, and b) higher in tumours that have metastasized, or are likely to (specification at, for example, page 19, last paragraph, pages 28-29; Figures 2 and 4, showing relative levels of 7a5/Prognostin expression in non-metastatic and metastatic tissues). In the subject application, the over-expression of 7a5/Prognostin is exemplified in a colon carcinoma model. The specification also teaches that 7a5/Prognostin expression can be used in the diagnosis of a variety of cancers.

The over-expression of 7a5/Prognostin in various types of cancer is evidenced by the experimental results set forth in the Expert Declaration of Dr. Ulrike Stein submitted herewith. These results show that 7a5/Prognostin is significantly over-expressed in cancer patients v. non-cancer patients. Expression is even higher in cancer patients who develop metastases compared to cancer patients who do not develop metastases. Such 7a5/Prognostin over-expression is observed in patients with, for example, colon cancer, breast cancer, colorectal cancer, rectal cancer, and gastric cancer (the Declaration of Dr. Stein, Figures 1-7). The results presented by Dr. Stein further establish that the applicants' method can be reliably performed as claimed by a person skilled in the art without the need for undue experimentation.

The practice of the claimed method requires no more than conducting routine procedures to determine 7a5/Prognostin expression as taught in the specification. Therefore, the full scope of the claims is enabled.

With regard to colorectal cancer, the Examiner notes that, in a manuscript previously submitted by the applicants (with their Response dated May 21, 2008), there does not appear to be a significant difference between expression of Prognostin in primary colorectal tumors and metastatic colorectal cancer cells. The applicants respectfully submit that this observation is entirely consistent with (and is, in fact, further evidence of) the utility and enablement of the

subject invention. Specifically, consistent with the invention as claimed, and as shown in Supplemental Figure 1 of that manuscript submitted with the previous Response, high Prognostin levels exist in metastases and in primary tumors that are likely to metastasize. On the other hand, primary cancer cells with lower levels of Prognostin, as shown in Figures 2 and 4 of the current specification, are less likely to produce metastases.

These different levels of expression (high expression correlating with metastatic tumors and cells, and lower expression in non-metastatic tumors and cells) are, in fact, a key to the claimed prognostic method. Thus, the applicants respectfully submit that Supplemental Figure 1 is actually further evidence of the enablement of the subject invention with respect to colorectal cancer.

With regard to diagnosis relating to breast cancer, the Office Action notes that the evidence submitted with the applicants' Response of January 21, 2009 was not in the form of a Declaration under 37 CFR §1.132. Accordingly, the applicants are submitting herewith such a Declaration executed by Dr. Stein. The results presented by Dr. Stein establish that the applicants' method can be readily, and without undue experimentation, performed by a person skilled in this art.

As demonstrated in the Declaration of Dr. Stein, experiments show that evidence of 7a5/Prognostin over-expression can be found in blood samples obtained from cancer patients (compared to non-cancer patients), and in cancer patients having metastasizing (including colon cancer, breast cancer, colorectal cancer, rectal cancer, and gastric cancer patients).

The over-expression of 7a5/Prognostin can be detected by routine methods known in the art. It is well recognized that circulating nucleic acids, especially cell-free mRNA, can be detected in plasma. By performing routine plasma-based expression profiling, tumor-derived mRNA transcripts in blood can be quantified.

Therefore, one skilled in the art could readily, and without undue experimentation, use the claimed methods for 1) predicting whether a tumor is likely to metastasize; and 2) diagnosing whether a subject has cancer. Accordingly, the full scope of the claims is enabled and the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph.

In view of the foregoing remarks and the amendments above, the applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

The applicants also invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephone interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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Attachment: Expert Declaration of Dr. Ulrike Stein under 37 CFR §1.132